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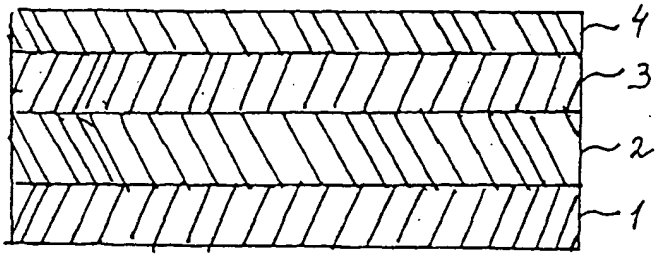
(54) Title: A MEDICAL DEVICE CONTAINING LIGHT-PROTECTED THERAPEUTIC AGENT AND A METHOD FOR FABRICATING THEREOF



(57) Abstract: Light- and/or UV-radiation protective coatings for drug delivery devices, such as, for instance, drug eluting vascular stents, where the drugs being delivered via the stents are light sensitive. A method of fabricating a medical article, such as a drug eluting vascular stent, that includes the light- and/or UV-radiation protective coating.

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addition, can have other important functions, such as providing the stent with increased lubricity and serve as an oxygen and/or water vapor barrier.

Currently, a typical embodiment used to achieve local drug delivery via stent comprises a stent coated with a three-layer composition shown on FIG. 1 and described subsequently. The three layer composition includes a drug-polymer layer 3, a primer polymer layer 2 for improving adhesion of the drug-polymer layer 3, and a topcoat polymer layer 4 providing rate limiting barrier, lubricity and other useful properties. The medicine to be administered according to this embodiment slowly seeps from the drug-polymer layer through the topcoat polymer layer to the diseased site in the patient's body where the stent is implanted.

However, such traditional composition has some drawbacks and disadvantages. One of the drawbacks and disadvantages is the fact that some of the drugs, which are currently being tested in the market, such as actinomycin-D, are very light sensitive and their therapeutic utility can be severely compromised, or even destroyed if they are exposed to light. Since the topcoat polymer layer is usually clear enough to allow light to pass through, the light-sensitive drug in the drug-polymer layer often needs special protection.

In order to protect the drug in the drug-polymer layer, the manufacturing of the coated stent must take place in the environment with filtered light, where the wavelengths which can negatively affect the drug have been filtered out.

the controlled-release tablets are provided with a light-protective coating in order to preserve the light-sensitive medicine from degradation.

As an example, Kanikanti, *et. al.* recommend spraying a water-based suspension of a film former, PEG (plasticizer), titanium dioxide and iron oxide (the light-scattering and absorbing pigments), followed by drying in hot air. Obviously, Kanikanti, *et. al.* use TiO_2 and Fe_2O_3 as light-protective compounds. However, Kanikanti, *et. al.* deal exclusively with tablets for oral administration. This reference does not describe nor suggest using light-protective compounds on stents. The difference in applications is quite substantial. In fact, a light protective coating for an oral tablet is fundamentally different than a light protective coating for an implantable device.

Using materials such as Fe_2O_3 to protect against light may be acceptable in the light protective coating for an oral tablet, but is not an acceptable method for the stent coatings because the stent coatings must be extremely inert and must not interfere with the body's inflammatory response in any way. Some experts have theorized that the etiology of restenosis is caused by inflammatory response. Materials ingested orally and which are subsequently excreted can be much more toxic than a material that is implanted in the tissues. In addition, the method described by Kanikanti, *et. al.* suggest using hot air to dry the light protective compound. In many cases the drug may be heat sensitive and cannot tolerate drying conditions at high temperatures. Moreover, for the tablets described by Kanikanti, *et. al.* there is no issue of post-processing raised by the inventors.

The usual method of protecting wood against damage by light without giving up the visual image of the wood surface to use a colorless polymer coating containing a light stabilizer, in particular a UV absorber. Valet, *et. al.* teach the use of a derivative of benzophenone as an UV absorber. Such compounds display a distinct stabilizer action against the effect of light, when applied in a coating composition.

Both Roberts, *et. al.* and Valet, *et. al.*, however, disclose only compositions where it is the outer surface of the substrate, be it rubber or wood, that is light-protected. These references do not teach the protection of the internal layers of the composition nor the protection of any light vulnerable fillers.

In addition, these references discuss protection solely from UV-radiation. The references do not describe a material having properties allowing for the protection of a light-sensitive drug, more specifically, a drug in an implantable device, where the protection is provided from both UV and/or visible light degradation. Yet a need to have such material is acute.

The present invention provides a number of such light- and/or UV-radiation protected coatings for implantable devices such as stents according to the following description.

SUMMARY OF THE INVENTION

This invention provides a light-protected polymer coating for medical devices, particularly, for medicated stents containing light-sensitive drugs.

destruction, thus ensuring the preservation of the therapeutical properties of the drug when it is incorporated in the stent.

According to one aspect of this invention, a coating for medical devices is provided, the coating having increased light resistance, the coating comprising a drug-polymer layer containing a drug included into the drug-polymer layer, and a light- and/or UV-protective compound incorporated into the coating.

According to another aspect of this invention, a coating for medical devices is provided, the coating having increased light resistance properties, the coating comprising a drug-polymer layer containing a drug incorporated into the drug-polymer layer, and a topcoat polymer layer, where a light- and/or UV-protective compound dispersed within the topcoat layer.

According to yet another aspect of this invention, a coating for medical devices is provided, the coating having increased light resistance properties and including a drug-polymer layer and a topcoat layer, where a film-forming polymer layer disposed upon the topcoat layer, and the light- and/or UV-protective compound is dispersed in the film-forming polymer.

According to another aspect of this invention, a coating for medical devices is provided, the coating having increased light resistance properties and including a drug-polymer layer, where light- and/or UV-protective compound is dispersed within the drug-polymer layer.

FIG. 2D schematically depicts a cross-section of an embodiment of this invention combining the features of the embodiments depicted in FIG. 2A and FIG. 2C.

FIG. 2E schematically depicts a cross-section of an embodiment of this invention combining the features of the embodiments depicted in FIG. 2B and FIG. 2C.

DETAILED DESCRIPTION OF THE EMBODIMENTS OF THE INVENTION

FIG. 1 shows a cross-section of a typical medical device 100 incorporating a polymer coating. This coating is currently known and used on medical devices, particularly, on stents. According to this embodiment, a stent 1 is coated with a primer polymer coating layer 2 and by a drug-polymer layer 3. The drug-polymer layer 3 comprises a polymer binder and a drug, dispersed in the binder, to be administered via the stent 1. Finally, a polymer topcoat layer 4 is applied on top of the drug-polymer layer 3 for controlling the rate of release of the drug.

As mentioned previously, the prior art system 100, shown on FIG. 1, allows for light rays to penetrate the topcoat layer 4 because this layer is typically clear and/or light-transparent. Consequently, the light reaches to the drug-polymer layer 3 and damages the drug, should the drug be light-sensitive. In fact, many of the drugs used with stents are light-sensitive.

bioabsorbable or biostable polymers could also be used with the embodiments of the present invention.

The first embodiment 200 is shown in FIG. 2A. It is similar to the prior art embodiment of FIG. 1 but an extra light-protective polymer layer 5 is applied on top of the topcoat polymer layer 4. The polymer in the layer 5 is typically one of the polymers commonly used for making topcoats. The layer 5 includes an compound which makes the layer 5 non-transparent. The use of the primer layer 2 in this and every other embodiment of this invention is optional. If a drug to be protected is predominantly sensitive in the UV-area, then known UV-absorbing compounds can be used, and if the sensitivity of the drug is chiefly in the visible range of wavelengths, then the compounds absorbing radiation in the visible area of the spectrum are used.

Typically, many important drugs are sensitive to radiation in both UV- and visible portions of the spectrum, and the drug-polymer layer can contain between about 5% and about 50% of the drug, by the mass of the drug-polymer layer 3.

Therefore, a compound to be used should provide protection from both UV-radiation and visible light. In addition, the compound should be compatible with the polymer in the drug-polymer layer 3 and compatible with the drug. Furthermore, the compound should be biologically compatible, so that when the device is implanted in a body, the compound will not produce any adverse responses. One of such compounds can be carbon black.

compound may also have a therapeutic effect such as reducing platelet adhesion and fibrinogen binding. In addition to a colorant, other light- and/or UV-radiation protective compounds can be selected by those ordinarily skilled in the, taking into account the functions and the amount of the drug, as well as the above-mentioned requirements of UV- and light-protection, biocompatibility and inertness.

The amount of solids in the layer 6 (the compound plus the polymer) can be between about 0.25% (mass) and about 20% (mass) of the solution to be applied to form the layer 6. Alternatively, the amount of solids can be between 1% (mass) and about 8% (mass). The ratio, by mass, of the light- and/or UV-radiation protective compound to the polymer is between about 3 to 1 (at the lower range of concentrations of the solution to be sprayed) and about 1 to 3 (at the higher range).

The thickness of the layer 6 can be within a range of between about 100 nanometers and about 4 micrometers, alternatively, between about 1 micrometer and about 2 micrometers.

In another embodiment 400 of this invention shown by FIG. 2C, the light- and/or UV-radiation protective compound is added to the drug-polymer layer 3'. The compound is added to a solution containing the drug and the polymer component of the drug-polymer layer 3' and the solution is applied onto the stent. This embodiment provides an additional advantage of shielding the UV- and/or light-sensitive drug during the process of applying the drug on the stent. Since the

embodiment 2C (having a drug-polymer layer 3' containing the light- and/or UV-radiation protective compound).

In the embodiment depicted on FIG. 2C using the topcoat layer 4 is optional, and the coating can remain viable when the drug-polymer layer 3' is the outermost layer. Furthermore, as mentioned previously, the use of the primer layer 2 is also optional. Therefore, the device of this invention can comprise just an implantable medical device coated with a drug-polymer coating containing a light- and/or UV-radiation protective compound. As another alternative, the device of this invention can comprise just an implantable medical device coated with a primer layer, on top of which the drug is applied without polymer, followed by a light- and/or radiation protective topcoat.

Either embodiment shown by FIGs. 2A, 2B or 2C can be used with any kind of the primer polymer layer 2, which would be otherwise usable, according to the criteria known to those having ordinary skill in the art. The thickness of the primer polymer layer 2 is not affected by the use of a protective layer of this invention and the method of application of the primer layer 2 remains the same.

The polymers used in either the embodiment of FIGs. 2A, 2B, and 2C, i.e., the drug-polymer layer 3, the topcoat layer 4, the protective layer 5, and the topcoat/protective polymer layer 6 are chosen according to the criteria known to those having ordinary skill in the art and as required by parameters such as the type of the device, the material of which the device is made, the type of process employed to form the coating, and a like.

cellulose nitrate, cellulose propionate, cellulose ethers, and carboxymethyl cellulose.

The drugs forming a part of the drug-polymer layer 3 are light-sensitive or UV-sensitive drugs, or both. Examples of such drugs include, for instance, actymicin D, paclitaxel, vincristine or other light or UV-sensitive drugs.

In every embodiment of this invention, each layer is applied by any appropriate method known to those ordinarily skilled in the art, for example, by spraying, or, alternatively, by dipping.

Having described the invention in connection with several embodiments thereof, modification will now suggest itself to those having ordinary skill in the art. As such, the invention is not to be limited to the described embodiments

7. The coating as claimed in Claim 6, wherein said light- and/or UV-protective compound is further dispersed within said drug-polymer layer.

8. The coating as claimed in Claim 5, further comprising a film-forming polymer layer disposed on said topcoat layer, wherein said light- and/or UV-protective compound is dispersed in said film-forming polymer layer.

9. The coating as claimed in Claim 1, wherein said light- and/or UV-protective compound is dispersed within said drug-polymer layer.

10. The coating as claimed in Claim 1, further comprising a primer polymer layer deposited between a surface of said medical device and said drug-polymer layer.

11. The coating as claimed in Claim 1, wherein said light- and/or UV-protective compound comprises carbon black or gold.

12. A method for fabricating a medical article, the method comprising forming a coating onto said medical device, wherein said coating includes light- and/or UV-protective substance.

13. A medical device comprising a coating, said coating produced according to the method of Claim 12.

14. The method as claimed in Claim 12, wherein said medical device is a stent.

22. The method as claimed in Claim 15, wherein said light- and/or UV-protective substance is dispersed within said drug-polymer layer.

23. The method as claimed in Claim 15, further comprising a primer polymer layer deposited between a surface of said medical device and said drug-polymer.

24. The method as claimed in Claim 15, wherein said light- and/or UV-protective substance comprises carbon black or gold.

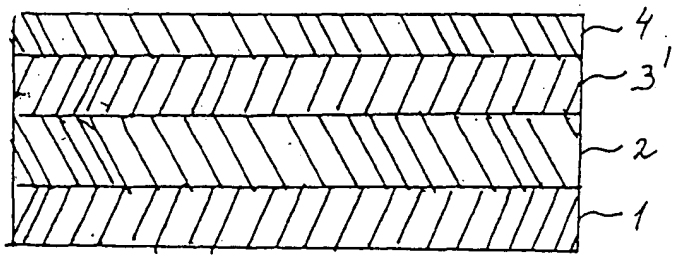

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FIG. 2C

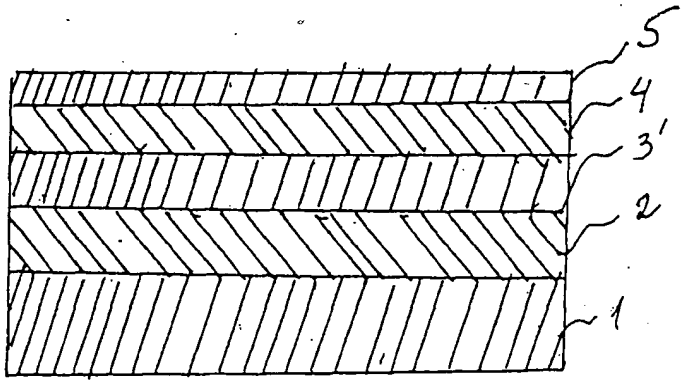

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FIG. 2D

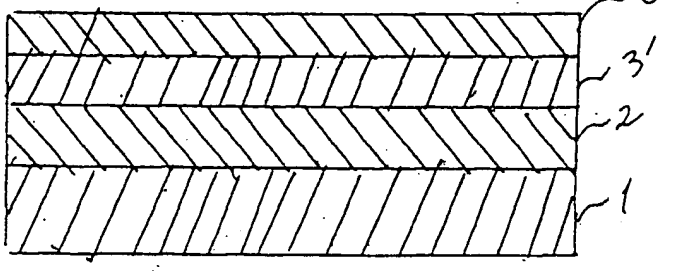

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FIG. 2E